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THE COUNCIL FOR TOBACCO RESEARCH–U.S.A., INC.

110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8885

Application for Research Grant

(Use extra pages as needed)

Date: 7/31/74

1. Principal Investigator (give title and degrees): Leonide Goldstein, D.Sc.
Associate Professor of Psychiatry

Co-Principal Investigator: Judith M. Nelsen, Ph.D.
Instructor in Psychiatry

2. Institution & address:

Department of Psychiatry
Institute of Mental Health Sciences
CMDNJ-Rutgers Medical School
P. O. Box 101
Piscataway, New Jersey 08854

3. Department(s) where research will be done or collaboration provided:

Department of Psychiatry

4. Short title of study:

The "Chronic Nicotine State" and Anxiety: A Behavioral and Electroencephalographic Analysis of Induced and Spontaneous Hyper-activation in Rats.

5. Proposed starting date: January 1, 1975

6. Estimated time to complete: One year

7. Brief description of specific research aims:

Because the present application represents the logical continuation of a line of research which has been developed in our laboratory with the aid of support from The Council, it might be useful to review some of the general considerations underlying our studies and the specific experimental goals already achieved which have led us to our current state and have suggested the paths which we would like to pursue. This background will be brief but a more detailed description may be found in the attached "Progress Report".

Electroencephalographic studies with rabbits and rats in our laboratory have indicated that chronic nicotine treatment results in changes in cortical-limbic-reticular formation relationships which might well modify an organism's functional state particularly in terms of the level and nature of arousal (Bhattacharya and Goldstein, Neuropharmacol. 9: 109-118, 1970 and Nelsen, Pelley, and Goldstein, Res. Comm. Chem. Pathol. and Pharmacol. 5: 694-704, 1973). The mesencephalic reticular activating system has long been implicated in the control of arousal. It has been demonstrated repeatedly that electrical stimulation of the mesencephalic reticular formation can produce cortical EEG activation and also, behavioral

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activation, for example, the awakening of a sleeping or sedated animal. In fact, we have in this laboratory recently demonstrated this phenomenon as is described in the attached "Progress Report". However, it is apparent that the reticular formation (RF) is not unique in its capacity to induce and maintain arousal. First, the EEG state of sleep which follows mid-collicular section is not necessarily permanent. Batsel (Electroencephal. Clin. Neurophysiol. 12: 421-430, 1960) and Villablance (Electroencephal. Clin. Neurophysiol. 19: 576-586, 1965) have described patterns of spontaneous EEG arousal followed by alternating states of sleep and wakefulness emerging 10 to 15 days after such surgical lesioning. Further, studies have shown that electrical stimulation of portions of the limbic system, particularly the amygdaloid nucleus and hippocampus can produce cortical EEG activation even in "cerveau isole" preparations (Carli, et al., Arch. Ital. Biol. 103: 725-750, 1965). This implies that arousal may be mediated by structures other than the reticular activating system, specifically limbic structures.

It has been suggested that the arousal mediated by the RF is non-specific or generalized in nature while that mediated by the limbic system allows for more selectively motivated or goal-directed behaviors and, further, that the RF and limbic systems are mutually inhibitory (Routtenberg, Psychol. Rev. 75: 51-80, 1968). The EEG studies conducted in our laboratory have indicated that chronic nicotine treatment induces a state of heightened limbic arousal or relatively greater limbic influence and lesser RF influence in the production of cortical activation (Bhattacharya and Goldstein; Nelsen, Pelley and Goldstein). From this finding, it was predicted that such a chronic nicotine state would be beneficial for performance of behaviors requiring focused attention or arousal and discrete goal-directed responses. Direct behavioral testing of this prediction confirmed that chronic nicotine treatment did improve performance of a visual attention task by rats (Nelsen and Goldstein, Psychopharmacologia 26: 347-360, 1972).

At appropriate current levels, delivery of short trains of electrical current to the RF disrupts on-going conditioned behavior presumably because the induced state is one of generalized over-arousal. If the RF and limbic system are mutually inhibitory, then one could hypothesize that the over-arousal or hyper-stimulated state resulting from increased RF activation could be counter-acted by increased limbic activation. In a preliminary study described at length in the "Progress Report", we have tested this hypothesis and found that nicotine was efficacious as an antagonist of the behavioral disruption resulting from RF stimulation. In effect, nicotine is capable of protecting (putatively, by increasing the level of limbic arousal) against an induced state of generalized, unfocused disruptive arousal (which might be considered an animal analog of anxiety) resulting from RF over-arousal. We are presently investigating nicotine's block of RF over-drive in an

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experimental situation which allows the simultaneous measurement of EEG activity and behavior on the visual attention task under conditions of RF electrical stimulation. Arrival at this stage of methodological sophistication has resulted from intensive efforts expended toward the development of appropriate technics and the acquisition of the required instrumentation. Reviewed in the "Progress Report" are the methodological advances made with the aid of past Council support. Important is the fact that we are now capable of characterizing more directly the affects of nicotine on the brain electrical events associated with arousal and with the acquisition and performance of behavioral tasks.

Our present research aims relate directly to the line of investigation reviewed. An underlying aim is to utilize animal models for the purpose of exploring some of the features of chronic nicotine administration which for ethical or procedural reasons, cannot be done effectively in humans. Our results, thus far, indicate that chronic nicotine treatment induces a central state which is optimal for carrying out specific learned, goal-directed behaviors. The recent data suggest that nicotine can protect from the behavioral disruption of electrically-induced RF over-drive. The obvious extension presents itself. The hypothesis is that chronic nicotine treatment should ameliorate the behavioral disruption resulting from spontaneous states of RF over-activation. We propose to test for the consequences of chronic nicotinization and withdrawal in rats separated into low anxiety and high anxiety or emotionality categories on the basis of baseline behavioral measures. If rats classified as highly anxious are in that state because of relative RF predominance in the control of arousal, then chronic treatment with nicotine should render them less sensitive to stress; i.e., they should be less susceptible to behavioral breakdown in anxiety-provoking situations than highly anxious rats not treated with nicotine. We propose to compare the relative effectiveness of the expected protection from behavioral disruption in rats with constitutionally different spontaneous arousal levels and to characterize the cortical and subcortical electroencephalographic indices of their functional states.

It has been suggested that withdrawal from the chronic nicotine state (cessation of habitual smoking in humans) is of itself stressful. One would predict that withdrawal would be far more traumatic for subjects constitutionally more anxious or emotional than for less anxious subjects. We propose to quantify the behavioral and electrophysiological consequences of withdrawal from the chronic nicotine state. Of particular interest will be indications of behaviors which might be interpreted as compensatory following cessation of nicotine. Specifically, by methods described in "Item 9", we intend to investigate differences in food consumption (body weight alterations) and spontaneous preferences for alcohol between the high and low anxiety animals during the withdrawal phase.

DAYS	PHASE	TEST	Hi Anxiety		Lo Anxiety	
			Saline	Nicotine	Saline	Nicotine
1	Testing and classification of all subjects into high and low amplitude categories					
14						
1	Treatment I					
7						
8		Control	X	X	X	X
9		Stress (CAT)	X	X	X	X
10						
11		Control	X	X	X	X
12		Stress (Aud. Stim)	X	X	X	X
13						
14						
15		Control	X	X	X	X
16		Stress (Foot-Shock)	X	X	X	X
17						
18		Control	X	X	X	X
19		Stress (RFS)	X	X	X	X
1	Withdrawal I (Body Wt. Monitoring)	Control	X	X	X	X
2		Control	X	X	X	X
3						
4		Control	X	X	X	X
5		Stress	X	X	X	X
6						
7						
8		Control	X	X	X	X
9		Control	X	X	X	X
10						
11		Control	X	X	X	X
12		Stress	X	X	X	X

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DAYS	PHASE	TEST	Hi Anxiety		Lo Anxiety	
			Nicotine	Saline	Nicotine	Saline
1	TREATMENT II					
7						
8		Repeat test	X	X	X	X
9		schedule men	X	X	X	X
10		for TREATMENT				
11		PHASE I	X	X	X	X
12			X	X	X	X
13						
14						
15			X	X	X	X
16			X	X	X	X
17						
18			X	X	X	X
19			X	X	X	X
1	WITHDRAWAL II (ETHANOL PREFERENCE)	Repeat test	X	X	X	X
2		schedule men	X	X	X	X
3		for WITHDRAWAL				
4		PHASE I	X	X	X	X
5			X	X	X	X
6						
7						
8			X	X	X	X
9			X	X	X	X
10						
11			X	X	X	X
12			X	X	X	X

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8. Brief statement of working hypothesis:

The state of arousal, its level and/or nature, is a critical feature in determining the direction and effectiveness of behavior. Chronic nicotine treatment produces shifts in the balance between reticular formational and limbic influences on arousal, yielding a state of enhanced "motivational (limbic) arousal" and reduced "drive (reticular) arousal". This brain functional state is the appropriate one for engaging in focused, goal-directed behavior. Chronic nicotine treatment should counter-act the behaviorally disruptive effects of induced and spontaneous states of reticular over-arousal.

9. Details of experimental design and procedures (append extra pages as necessary)

The experimental procedures which are followed for the preparation of animals with chronic recording and stimulating electrodes, for recording and analysing brain electrical activity, for stimulating discrete brain areas, and for training and testing animals on the visual attention task have been described in previous proposals to The Council. These procedures are included in the attached "Progress Report" and will not be repeated here. However, there are two procedural conventions which we have adopted in past studies of nicotine in the rat and which will be incorporated in future studies. The first concerns the choice of an appropriate dose level. Our studies have always been aimed at investigating behavioral and electrophysiological effects of nicotine which might relate to and, in fact we would hope, lead to a better understanding of the mechanisms of arousal and of the motivations accounting for the widespread self-administration of nicotine by humans. Accordingly, we have chosen dose levels which are considered behavioral (not toxicological) and which co-respond to levels attained when nicotine is self-administered by smokers. The second convention is really related to the first, because it involves the dosage regime and testing schedule. Humans smoke chronically, so that it seems most reasonable that electrophysiological and behavioral information collected in subhuman species will be most meaningful for extrapolation if the chronic, not the acute effects of nicotine are the focus. Further, it has been clearly demonstrated by studies in this laboratory that the effects of acute nicotine administration are very different from those of chronic administration both in terms of behavioral and electroencephalographic responses. Some of these differences and the explicit importance of an awareness of them are described in the attached manuscript of a paper presented at the 1974 meeting of the Behavioral Pharmacology Society. The point is that our studies are designed to elucidate chronic treatment effects.

It has been demonstrated that high and low emotionality strains of rats will respond differentially to treatment with various psycho-active drugs (e.g., Gupta and Holland, Neuropharmacology 11: 31-38, 1972). Further, within a strain which has not been specially bred for emotionality levels,

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it is possible to separate out more highly emotional or anxious animals from low anxiety animals. These subgroups respond differentially to drugs according to behavioral measures. Recently, a method of classifying rats as having high emotionality or low emotionality according to their initiation of consummatory behavior in an open field has been described (Mollenauer, Plotnik and Snyder, Pharmacology, Biochemistry and Behavior 1: 509-514, 1973). This test situation seems to be eminently appropriate for exploring some of the effects of nicotine which should be characterized. Briefly, rats are food deprived for 23 hours before being tested in a circular arena which is marked off in concentric circles and spokes. In the center of the area is a mesh cylinder which can serve as a cat enclosure for stress tests. Four drinking cups are placed, equally spaced, five cm. away from the central mesh enclosure. These cups contain a 32% sucrose solution. Rats are classified for their constitutional level of emotionality according to their readiness to approach and to consume the sweetened water. A pilot study will be run in our laboratory, but other investigators have found it effective to label rats which have not initiated drinking before the fifth testing day (5 minute tests each day) as high emotionals and those which have initiated drinking as low emotionals. The measures which serve as indices of relative levels of anxiety are: (1) cumulative drinking time; (2) approach or cumulative time with the two front feet in the concentric circle nearest the central enclosure; (3) total number of lines crossed; and (4) freezing or cumulative time spent rigidly immobile.

With continued training, differences between groups tend to "wash out", but when exposed to stress or anxiety-provoking stimuli in the test arena, the high anxiety and low anxiety group differences re-emerge. We intend to use this behavioral situation to test for the possible protection provided by chronic nicotine against disruption produced by stressful stimuli and to index the effects of nicotine withdrawal on high and low anxiety subjects. Approximately 50 Holtzman, Sprague-Dawley male rats will be trained and classified as high or low anxiety subjects according to the procedure described above. Members of these two groups will be divided randomly into two subgroups. One of each of the pairs of subgroups will receive chronic nicotine treatment (100 ug/kg, t.i.d., s.c.) and the other chronic saline treatment. The solutions will be coded so that the experimenters will be "blind" insofar as which treatment a subject is receiving. Rats will be maintained on the chronic injection schedule for seven days to insure the development of the chronic nicotine state. Animals will be tested four days a week according to the schedule outlined on the attached table (Treatment Phase I). In each case, a "control test" day will precede a "stress test" day. Rats will be subjected to four types of stress in order to assess the protective efficacy of nicotine as it relates to constitutional or baseline levels of anxiety.

These are:

1. Presence of a cat in the screened core of the experimental apparatus.

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2. Aversive auditory stimulation emanating from the screened core of the arena.

3. A short course of unavoidable foot-shock administered in a separate chamber, three minutes before testing in the experimental arena.

4. Reticular formation stimulation delivered to subgroups which will be specially prepared with chronic recording and stimulating electrodes in the brain.

At this point, the injection schedule will be terminated and the Withdrawal Phase I initiated. This phase will be carried out for two weeks. Four test sessions will be conducted each week, three of them control sessions and one, a stress test session. During the period of withdrawal, careful monitoring of body weights will be done. The animals must be partially food deprived to be motivated to drink in the experimental field (23 hours of food deprivation), but a major focus of attention during this phase will be differences in food consumption during the hour of free access to food and water immediately following the test session. In order to discriminate any changes in eating patterns, each animal will be weighed immediately before testing, tested, given free access to food and water for one hour, and then weighed again. Following Withdrawal Phase I, Treatment Phase II will begin. The same treatment and testing schedule followed in the first treatment phase will be repeated, this time with the groups "crossed-over" so that each animal will receive the treatment it had not received during Treatment Phase I. Withdrawal Phase II will follow, during which monitoring of body weights will be done, but additionally, testing will be conducted to discriminate whether differential development of spontaneous ethyl alcohol drinking behavior will be exhibited between treatment and anxiety-level groups.

We are currently investigating the most effective technics to measure tendencies toward spontaneous alcohol consumption and are fortunate in having available the advice of workers at the Center for Alcohol Studies which is located on the same campus as is the Rutgers Medical School.

An important feature of this proposed study is that electroencephalographic measures will be made on certain surgically prepared members of the experimental groups. Because of the logistical prohibitions involved in preparing with chronic brain electrodes and recording from 50 animals, twelve will be chosen out and monitored for electrophysiological effects during the study. Methodological developments in our laboratory (see Progress Report) will allow us to carry out such recording and to further characterize the central nervous system mechanisms operating under conditions of high and low anxiety and the modifications which nicotine provides insofar as these central mechanisms and behavior are concerned.

10. Space and facilities available (when elsewhere than item 2 indicates, state location):

The laboratory unit is comprized of four specially designed rooms, two of which are 10.5' x 16.5' and two, 9' x 10'. There are also three offices, 10.5' x 12.5'. One of the larger rooms is equipped for behavioral experimentation and the other electroencephalographic recording.

Animal care and maintenance is provided on a per diem basis at the Vivarium of the Rutgers Medical School. A full-time veterinarian supervises the facility.

A Model 1766 Monroe Desk Computer is available for much of the data analysis required for this project. Further, services of the Rutgers University computer are available via a terminal maintained in our building.

11. Additional facilities required: None

12. Biographical sketches of investigator(s) and other professional personnel (append): See attached

13. Publications: (five most recent and pertinent of investigator(s); append list, and provide reprints if available).
See attached. Significant reprints are enclosed. More copies of the "review chapter" will be sent when available.

14. First year budget:

A. Salaries (give names or state "to be recruited")	% time	Amount
Professional (give % time of investigator(s) even if no salary requested)		
Leonide Goldstein, D.Sc., P.I. Judith M. Nelsen, Ph.D., Co-P.I.		REDACTED
Technical		
Kathleen Pelley, B.A.		REDACTED
Secretary		
	Sub-Total for A	REDACTED

B. Consumable supplies (by major categories)	
Chart and Printer tapes	500.00
Animals (purchase and care)	1,050.00
Chemicals, drugs and electrode equipment	600.00
Sub-Total for B	2,150.00

C. Other expenses (itemize)	
Travel	500.00
Publication costs	500.00
Sub-Total for C	1,00.00
Running Total of A + B + C	37,686,59

D. Permanent equipment (itemize):	
Behavioral modules	400.00
Open field arena	150.00
Sub-Total for D	550.00
E	5,652.99
Total request	$43,889.58

E. Indirect costs (15% of A+B+C)

15. Estimated future requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Indirect Costs	Total
Year 2						
Year 3						

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5.

16. Other sources of financial support:
List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
A Study of EEG Correlates of Cognitive Modes	GRS (NIH)	$2,500.00	7/1/74-6/30/75

PENDING OR PLANNED

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
Effect of Microwaves on the EEG and Behavior of Animals	BRH-FDA	$38,000.00	9/1/74-8/31/74

It is understood that the investigator and institutional officers in applying for a grant have read and accept the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Checks payable to

Mailing address for checks

Principal investigator

Typed Name Leonide Goldstein, D.Sc.

Signature Leon Goldstein Date 7/31/74

Telephone 201 564 - 4416
Area Code Number Extension

Responsible officer of institution:

Typed Name Mr. Harold G. Logan

Title Acting Dean

Signature _____ Date 7/31/74

Telephone 201 564 - 4545
Area Code Number Extension

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Curriculum Vitae

Leonide Goldstein, D.Sc.

Born: REDACTED

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1921-35	Student at the Conservatoire National de Musique, Paris
1935	Graduated in violin, harmony and composition
1935-36	R R
1936-37	Technical Assistant Institut de Biologie, Paris
1937-39	Research Assistant
1939-40	R R
1940	Undergraduate studies, University of Paris
1941-42	Research Associate Laboratoire de Physiologie School of Medicine, University of Montpellier, France
1942	Member of the Research Division of the Free French Forces
1942-45	Special assistant to Dr. H.J. Muller, Amherst College, Amherst, Mass.
1944	B.A. and M.A. Amherst College
1945-47	Assistant Professor University of Paris (Physiology and Genetics)
1947-53	Acting Director Laboratoire de Biometrie of the French National Research Council
1951	Doctor of Sciences degree, University of Paris, Sorbonne
1953-58	Assistant Professor, Neurophysiology, Ecole Pratique des Hautes Etudes, Sorbonne.
1958-61	Associate Professor, Pharmacology, Emory Univ., Atlanta, Ga.
1961-64	Neuropharmacologist, Bureau of Research, Neuropharmacology Section, N.J. Neuropsychiatric Institute, Princeton, N.J.
1964-72	Research Scientist Grade 1, Bureau of Research, Neuropharmacology Section, N.J. Neuropsychiatric Institute, Princeton, N.J.
1969-73	Visiting Senior Fellow - Department of Biology - Princeton Univ.
1972	Associate Professor of Psychiatry, Rutgers Medical School, Piscataway, N.J.
1973	Member Graduate Faculty, Rutgers University, New Brunswick, N.J.
1973	Member Psychobiology Area Graduate Program in Psychology, Rutgers University, New Brunswick, N.J.
1974	Member of the Council Eastern Psychiatric Association.

Membership in Scientific Societies:

REDACTED

REDACTED

Honors:

Croix de Guerre (1939-40): Medal of the Free French Forces: Palmes Academiques (1950). Associate Editor "Research Communications in Chemical Pathology and Pharmacology." Member Examination Board French University Studies in the U.S.

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Listings:

American Men at Science - Who is Who.

Publications:

Author or co-author of 160 papers and abstracts.

PUBLICATIONS

Goldstein, L., Psychotropic drug-induced EEG changes as revealed by the amplitude integration method in "Psychotropic Drugs and the Human EEG". T. Itil, ed. S. Krager, New York (1974) pp. 58-74.

Goldstein, L., and Stoltzfus, N.W. Psychotropic drug-induced changes in interhemispheric EEG amplitude relationships in Agents and Actions 3, 124-132 (1973).

Goldstein, L., and Nelsen, J.M. Some views on the neurophysiological and neuropharmacological mechanisms of storage and retrieval of information in "Memory Transfer of Information", H.P. Zippel, ed. Plenum Publ. Corp., New York (1973) pp. 155-191.

Nelsen, J.M., and Goldstein, L. Chronic nicotine treatment in rats. I. Acquisition and performance of an attention task. Research Comm. Chem. Pathol. Pharmacol., 5, 681-693 (1973).

Nelsen, J.M., Pelley, K., and Goldstein, L. Chronic nicotine treatment in rats. II. Electroencephalographic amplitude and variability changes occurring within and between structures. Research Comm. Chem. Pathol. Pharmacol. 5, 694-704 (1973).

Nelsen, J.M., and Goldstein, L. Acquisition and performance of an attention task by rats subjected to chronic nicotine treatment. Fed. Proc. 32, 817 (1973).

CURRICULUM VITAE

Judith M. Nelsen, Ph.D.

BORN: REDACTED

MARITAL STATUS: REDACTED

1946-60	Primary and secondary studies, public schools of Town of Lake and City of Cudahy, Wisconsin
1960-63	Undergraduate studies, University of Wisconsin-Milwaukee (Letters and Science, Pharmacy)
1963	Laboratory assistantship in bacteriology (University of Wisconsin-Milwaukee)
1963-65	Undergraduate studies, University of Wisconsin- Madison (Pharmacy, Psychology)
1963-65	Research assistantship in physical chemistry (University of Wisconsin-Madison)
1964	Summer research assistantship in physical chemistry (from the U.S. Department of the Army at the University of Wisconsin-Madison)
1965	B.S. (HONORS) degree. University of Wisconsin. Madison, Wisconsin
1965-70	Graduate studies, Boston University School of Medicine, Division of Medical Sciences, Department of Pharmacology an Experimental Therapeutics (Major professor: Conan Kornetsky, Ph.D., Director, Laboratory of Behavioral Pharmacology)
1965-66	Graduate School Research Fellowship
1966-70	Public Health Service Research Fellowships (N.I.M.H.)
1970	Doctor of Philosophy degree. Boston University. Boston, Mass.
1970-72	Post-doctoral appointment. N.J. Bureau of Research in Neurology and Psychiatry. Box 1000, Princeton, N.J.
1973	Senior Scientist. Rutgers Medical School. Department of Psychiatry, Piscataway, N.J.

HONORS: Sophomore Honors (U.W.); Senior Honors (U.W.); Sigma Epsilon Sigma (U.W.); Rho Chi (U.W.); Phi Kappa Phi (U.W.); Sigma Xi (B.U.)

PROFESSIONAL SOCIETY MEMBERSHIPS:

REDACTED

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PUBLICATIONS

Nelsen, Judith M. and Conan Kornetsky: Single Dose Tolerance to Morphine Sulfate: EEG Changes. The Pharmacologist 10: No. 2, 1968.

Weil, Andrew T., Norman E. Zinberg, and Judith M. Nelsen: Clinical and Psychological Effects of Marihuana in Man. Science 162: 1234-1242, 1968.

Nelsen, Judith M. and Leonide Goldstein: Improvement of Performance on an Attention Task with Chronic Nicotine Treatment in Rats. The Pharmacologist 13: No. 2, 1971.

Nelsen, Judith M. and Leonide Goldstein: Improvement of Performance on an Attention Task with Chronic Nicotine Treatment in Rats. Psychopharmacologia 26: 347-360, 1972.

Nelsen, Judith M. and Conan Kornetsky: Morphine-Induced EEG Changes in Central Motivational Systems: Evidence for Single-Dose Tolerance. Fifth International Congress on Pharmacology (Abstracts, p. 166, #993), 1972.

Goldstein, Leonide and Judith M. Nelsen: Some Views on the Neurophysiological and Neuropharmacological Mechanisms of Storage and Retrieval of Information. In: Memory and Transfer of Information (H.P. Zippel, ed.). Plenum Press, New York, 1973, pp. 155-191.

Nelsen, Judith M.: Neurophysiological and Behavioral Consequences of Chronic Nicotine Treatment. In: Drug Addiction, vol.III (J.M. Singh, L.H. Miller, H. Lal, eds.). Futura Publishing Co., Mount Kisco (N.Y.), 1973 (Chapter accepted for publication).

Nelsen, Judith M. and Leonide Goldstein: Chronic Nicotine Treatment in Rats: 1. Acquisition and Performance of an Attention Task. Res. Comm. Chem. Pathol. and Pharmacol. 5: 681-693, 1973.

Nelsen, Judith M., Kathleen Pelley, and Leonide Goldstein: Chronic Nicotine Treatment in Rats: 2. Electroencephalographic Amplitude and Variability Changes Occurring Within and Between Structures. Res. Comm. Chem. Pathol. and Pharmacol. 5: 694-704, 1973.

PUBLICATIONS

Nelsen, Judith M. and Leonide Goldstein: Acquisition and Performance of An Attention Task by Rats Subjected to Chronic Nicotine Treatment. Fed. Proc. 32: 817, 1973.

Nelsen, Judith M.: Nicotine Tolerance: Electroencephalographic Activation and "Behavioral Depress". Paper before Behavioral Pharmacology Society, May 11, 1974, Columbia, Maryland.

Nelsen, Judith M., Kathleen Pelley and Leonide Goldstein: Protection by Nicotine of Behavioral Disruption Caused by Reticular Formation Stimulation in the Rat. In preparation.